R E M A R K S

Claim Amendments and New Claims

Claims 1, 4, 5 and 8 were canceled.

New claim 11 includes features of previous claim 1.

New claim 12 includes features of previous claims 1 and 4.

New claim 13 includes a feature of previous claim 12.

New claim 14 includes features of previous claim 5.

New claim 15 includes features of previous claims 5 and 8.

New claim 16 includes a feature of previous claim 5.

Obviousness Rejection Under 35 USC 103

Claims 1, 4, 5 and 8 were rejected under 35 USC 103 as being unpatentable over Dean et al. (USP 6,166,073) in view of The Patent Abstract of Japan and Hellberg et al. (USP 6,646,001) for the reasons set forth on page 3 of the Office Action.

Based on a June 25, 2009 telephone interview between the undersigned and the Examiner, it was clarified that the aforementioned Patent Abstract of Japan was JP 62-277323.

It was admitted in the Office Action that Dean et al. do not teach tonicity agents such as glycerin, polyethylene glycol, propylene glycol, mannitol, trehalose or sucrose.

Dean et al. (USP 6,166,073) relates to a composition for treating ocular hypertension comprising a combination of a DP-agonist prostaglandin and a FP-agonist prostaglandin. Example 1 in column 8 of Dean et al. describes a composition comprising FP-agonist prostaglandins such as latanoprost and benzalkonium chloride.

As described on page 2, lines 9 to 25 of the present specification, the benzalkonium chloride used in Dean et al. (BAK: $[C_6H_5CH_2N(CH_3)_2R]Cl$) is a mixture of compounds having various chain lengths of R(alkyl group). In contrast thereto, $[C_6H_5CH_2N(CH_3)_2R]Cl$, as recited in applicants' present claims (wherein R is an alkyl group having 12 carbon atoms), is not a composition, but a single compound. The aim of the presently claimed invention is to prevent white turbidity due to a change of formulation in an ophthalmic solution containing latanoprost having a concentration of 0.005% (W/V) by adding 0.003 to 0.01% (W/V) $[C_6H_5CH_2N(CH_3)_2R]Cl$, wherein R is an alkyl group having 12 carbon atoms. Dean et al. do not describe or suggest the problem of white turbidity due to a change of formulation in an ophthalmic solution containing latanoprost by benzalkonium chloride (BAK: $[C_6H_5CH_2N(CH_3)_2R]Cl$).

Table 1 on page 18 of the present specification and Table 5 on page 24 of the present specification show that white turbidity in a latanoprost ophthalmic solution is observed in the case where the concentration of BAK is 0.01% or 0.005%. In the DECLARATION UNDER 37 CFR 1.132 of Hiroyuki ASADA dated January 20, 2009 ("January 20, 2009 ASADA DECLARATION"), additional experiments were carried out following the same procedure as in Experiment 1-1) of the present specification for the case where the concentration of BAK is 0.007% or 0.003%. The following Table (a) shows the results set forth in the January 20, 2009 ASADA DECLARATION.

Table (a)

	Comparative formulation A-1	Comparative formulation A-2
Latanoprost	0.005	0.005
Crystalline sodium dihydrogenphosphate	0.2	0.2
Sodium chloride	0.9	0.9
BAK	0.007	0.003
Diluted hydrochloric acid	q.s.	q.s.
Sodium hydroxide	q.s.	q.s.
Purified water	q.s.	q.s.
Appearance	White turbidity	Slightly white turbidity

(Unit in Table: % (W/V), q.s.: quantum sufficient)

Tables 1 to 5 on pages 18 and 24, respectively, of the present specification, and Table (a) in the January 20, 2009 ASADA DECLARATION show that white turbidity was observed in a latanoprost-containing ophthalmic solution containing BAK having a concentration of 0.01%, 0.007%, 0.005% or 0.003%.

Table 3 on page 20 of the present specification and Table 7 on page 25 of the present specification show that white turbidity in a latanoprost ophthalmic solution is prevented by replacing BAK (0.01% and 0.0005%) with BAK-C_{12} ($[C_6H_5N(CH_3)_2R]Cl$, wherein R is an alkyl group having 12 carbon atoms) (0.01% and 0.0005%). In the January 20, 2009 ASADA DECLARATION, additional experiments were carried out following the same procedure as in Experiment 1-3) of the present specification for the case where the concentration of $[C_6H_5CH_2N(CH_3)_2R]Cl$, wherein R is an alkyl group having 12 carbon atoms is 0.007% or 0.003%. The following Table (b) shows the results set forth in the January 20, 2009 ASADA DECLARATION.

Table (b)

	Formulation B-1	Formulation B-2
Latanoprost	0.005	0.005
Crystalline sodium dihydrogenphosphate	0.2	0.2
Sodium chloride	0.9	0.9
BAK-C_{12}	0.007	0.003
Diluted hydrochloric acid	q.s.	q.s.
Sodium hydroxide	q.s.	q.s.
Purified water	q.s.	q.s.
Appearance	Colorless and Transparent	Colorless and transparent

(Units in Table: % (W/V), q.s.: quantum sufficient)

As apparent from the above Table (a) and Table (b), it has been confirmed that white turbidity is effectively prevented when adding 0.007% and 0.003% of $[C_6H_5CH_2N(CH_3)_2R]Cl$, wherein R is an alkyl group having 12 carbon atoms.

It is respectfully submitted that one of ordinary skill in the art would not consider that Dean et al. would provide the above-described advantageous results.

Hellberg et al. (USP 6,646,001) relate to a composition for treating ocular hypertension comprising a prostaglandin FP receptor agonist and a prostaglandin synthesis inhibitor. Example 2 in column 9 in Hellberg et al. describes a composition comprising latanoprost, benzalkonium chloride and mannitol. In contrast to

Hellberg et al., none of the nonionic tonicity agents recited in applicants' new claims 12 and 14 are described or suggested in Hellberg et al.. Moreover, it is respectfully submitted that Hellberg et al. do not teach or suggest the problem of white turbidity due to a change of formulation, and thus fail to teach or suggest a solution to such problem.

Thus, it is respectfully submitted that one of ordinary skill in the art would not arrive at applicants' claims 12 and 14 from Hellberg et al.

Further, although Example 4 of Hellberg et al. describe a composition comprising latanoprost and benzalkonium chloride (BAK: $[C_6H_5CH_2N(CH_3)_2R]C1$), for the same reason discussed above as in the case of Dean et al., it is respectfully submitted that one of ordinary skill in the art would not conceive of applicants' claims 11 and 13 from Hellberg et al.

As discussed above, Dean et al. and Hellberg et al. do not describe or suggest a single compound $[C_6H_5CH_2N(CH_3)_2R]C1$, wherein R is an alkyl group having 12 carbon atoms and nonionic tonicity agents such as glycerin, polyethylene glycol, propylene glycol, trehalose and sucrose, as recited in applicants' present claims. Dean et al. and Hellberg et al. also do not teach or suggest the

problem of white turbidity due to a change of formulation and thus do not teach or suggest a solution to such problem. Thus, it is respectfully submitted that one of ordinary skill in the art would not arrive at applicants' present claims from the combination of Dean et al. and Hellberg et al.

The Patent Abstract of Japan does not describe or suggest latanoprost.

It is therefore respectfully submitted that there is no reason to combine the cited references to attempt to arrive at applicants' presently claimed invention.

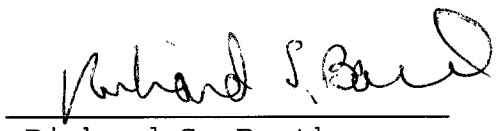
Withdrawal of the 35 USC 103 rejection is accordingly respectfully requested.

Reconsideration is requested. Allowance is solicited.

The USPTO fee of $220 for one additional independent claim is being paid by credit card herewith. Any additional fees or overpayments are hereby authorized to be charged to Deposit Account No. 06-1378.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



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